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(54) Title: PROCESS FOR THE PREPARATION OF CRYSTALLINE NANO-PARTICLE DISPERSIONS

(57) Abstract: A process for the preparation of a dispersion of crystalline nano-particles in an aqueous medium comprising combining (i) a first solution comprising a substantially water-insoluble substance in a water-miscible organic solvent with; (ii) an aqueous phase comprising water and optionally a stabiliser, to form a dispersion of amorphous particles; and (iii) sonicating the dispersion of amorphous particles for a sufficient period to form crystalline nano-particles of the substantially water-insoluble substance. The process provides nano-crystals with a mean hydrodynamic diameter of less than 1 micron, particularly less than 300 nm and is particularly useful for the preparation of nano-crystalline dispersions of pharmaceutical substances.

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INTERNATIONAL SEARCH REPORT

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iB 03/03044 A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61K9/10 A61 A61K9/14 A61K9/51 According to International Patent Classification (IPC) or to both national classification and IPC B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) A61K Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, WPI Data, PAJ C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. X.P US 2003/059472 A1 (DOTY MARK ET AL) 1-14,16, 17 27 March 2003 (2003-03-27) claims 1-6,18,25-33,43-47,51-62; figure 1 X WO 99 00113 A (MAGDASSI SHLOMO ; SAHADEVAN 1-6,11, DAVID C (US); SOON SHIONG PATRICK (US);)
7 January 1999 (1999-01-07) 12,14,17 page 9, paragraph 2; claims 53,61,62; example 19 page 21, paragraph 2 -page 22, line 21 page 35 X WO 98 14174 A (SOON SHIONG PATRICK ; TAO 1-5,11, CHUNLIN (US); YANG ANDREW (US); DESAI NEI) 9 April 1998 (1998-04-09) 14,16,17 page 10, paragraph 3; claims 1,12,21-27,36; example 2 page 18, paragraph 2 Further documents are listed in the continuation of box C. X Patent family members are listed in annex. Special categories of cited documents : "T" later document published after the international filing date or priority date and not in conflict with the application but clied to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) document of particular relevance; the delimed Invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. document referring to an oral disclosure, use, exhibition or other means document published prior to the international filing date but later than the priority date claimed *&* document member of the same patent family Date of the actual completion of the International search Date of mailing of the international search report 25 November 2003 04/12/2003 Name and mailing address of the ISA Authorized officer European Palent Office, P.B. 5618 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3018 Kardas-Llorens, E

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INTERNATIONAL SEARCH REPORT

In Ional Application No

	INTERNATIONAL SEARCH REPORT	FGB 03/03044					
C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT							
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.					
X	RUCH F ET AL: "Preparation of micrometer size budesonide particles by precipitation" JOURNAL OF COLLOID AND INTERFACE SCIENCE, ACADEMIC PRESS, NEW YORK, NY, US, vol. 229, no. 1, 1 September 2000 (2000-09-01), pages 207-211, XP002253141 ISSN: 0021-9797 cited in the application 2.Experimental	1,3-12, 14,17					
X	SJOESTROEM B ET AL: "THE FORMATION OF SUBMICRON ORGANIC PARTICLES BY PRECIPITATION IN AN EMULSION" JOURNAL OF DISPERSION SCIENCE AND TECHNOLOGY, NEW YORK, NY, US, vol. 15, no. 1, 1994, pages 89-117, XP009002392 ISSN: 0193-2691 Abstract page 95; table 1	1-7,10, 12,14, 16,17					
X	SJOSTROM B ET AL: "A METHOD FOR THE PREPARATION OF SUBMICRON PARTICLES OF SPARINGLY WATER-SOLUBLE DRUGS BY PRECIPITATION IN OIL-IN-WATER EMULSIONS. II: INFLUENCE OF THE EMULSIFIER, THE SOLVENT, AND THE DRUG SUBSTANCE" JOURNAL OF PHARMACEUTICAL SCIENCES, AMERICAN PHARMACEUTICAL ASSOCIATION. WASHINGTON, US, vol. 82, no. 6, 1 June 1993 (1993-06-01), pages 584-589, XP000367863 ISSN: 0022-3549 Abstract	1-8, 10-12, 14,16,17					
•							

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

nformation on patent family members

In that Application No I iB 03/03044

	···				f iB	03/03044
Patent document cited in search report		Publication date	Patent family member(s)		Publication date	
US 2003059472	A1	27-03-2003	MO	03026611 A2		03-04-2003
WO 9900113	Α	A 07-01-1999	US	609633	1 A	01-08-2000
			ΑU	8266298		19-01-1999
			BR	981094		05-02-2002
			CN	1267214		20-09-2000
			EP	1023050		02-08-2000
			ĤŪ	0003972		. 28-08-2001
			JP	200250797		12-03-2002
			NO	996433		14-02-2000
			NZ	502500		28-03-2002
			WO	9900113		07-01-1999
•			US	6537579		25-03-2003
•			US	2003199425		23-10-2003
			US	2003073642		17-04-2003
•			US	2003068362	AI	10-04-2003
			US	2003133955 6506405		17-07-2003
		·		0500403		14-01-2003
WO 9814174	Α	09-04-1998	US	5916596	5 A	29-06-1999
			AU	718753		20-04-2000
			AU	4592997		24-04-1998
			BR	9711856		06-11-2001
			CN	1237901	. A	08-12-1999
			EP	0961612	A1	08-12-1999
			JP NO	2001501931		13-02-2001
•			NZ	991620 335133		01-06-1999
			WO	9814174		22-12-2000
			US	2003068362		09-04-1998
			US	2003008362	A1	10-04-2003 17-07-2003
		,	ÜS	6537579		25-03-2003
						とり こりつこといいろ
			US	6506405		14-01-2003